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CAPUTA, EXAMINER

18N1/0920

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1813	24

DATE MAILED: 09/20/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3/14/95 (6/20/95, 3/8/95) ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-3, 10-26, 46, 47, 50-58 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 4-9, 27-45, 48, a-149 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-3, 10-26, 46, 47, a-150-58 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

Part III DETAILED ACTION

1. Applicants' amendment and declarations were received and been have entered. Claims 4-9, 27-45, 48, and 49 have been canceled. Claims 1-3, 10-26, 46, 47, 50-58 and are pending.

2. The text of those sections of Title 35 U.S.C. not included in this action can be found in a prior Office Action.

3. The prior objection to the title is withdrawn in view of applicants' amendment.

4. The prior objection to the use of trademarks is withdrawn upon further consideration by the Examiner.

5. The prior rejection of claims 1-3, 10-26, 46, and 47 are rejected under 35 U.S.C. § 112, second paragraph, is withdrawn in view of applicants' amendment.

6. The prior rejection of claims 1-3, 10-12, and 15-18 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of applicants' arguments.

7. The prior rejection of claims 15-26 under 35 U.S.C. § 101 and § 112, first paragraph because the claimed invention as disclosed lacks patentable utility is withdrawn in view of applicants' declarations.

The declarations by Drs. Kreider, and Schlegel under 37 C.F.R. § 1.132 filed March 8, 1995 and June 3, 1994 respectively are sufficient to overcome the rejection of claims 15-26 under U.S.C. § 101 rejection and 35 U.S.C. § 112, first paragraph for

failure to teach how to use of the L1 of human papillomavirus (HPV) as a vaccine in humans.

8. The prior objection to the specification and rejection of claims 1-3, 10-26, 46, 47, 50-58 under 35 U.S.C. § 112, first paragraph for failing to provide guidance to antigenic fragments capable of binding to conformation specific epitopes (see Section c) is withdrawn in view of applicants' amendment.

9. The prior rejection of claims 1-3, 10-26, 46, and 47 are rejected under 35 U.S.C. § 112, first paragraph (see Sections f and g) is withdrawn in view of applicants' amendment and arguments.

10. The prior rejection of claims 1-3, 10-26, 46, and 47 rejected under 35 U.S.C. § 103 as being unpatentable over Pilacinski et al., and further in view of Sambrook et al., Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270) is withdrawn in view of applicants' arguments and declaration.

The declaration by J. Suzich under 37 C.F.R. § 1.132 filed March 8, 1995 is sufficient to overcome the rejection of claims 1-3, 10-26, 46, and 47 based upon the teachings of Pilacinski et al. and further in view of Sambrook et al., Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270)

11. The prior rejection of claims 1-3, 10-12, 15, 18, 46, and 47 under 35 U.S.C. § 103 as being unpatentable over Zhou et al (J. Virology 185: 251-257 November, 1991) is withdrawn in view of applicants' declaration.

The declaration by Dr. Jenson under 37 C.F.R. § 1.132 filed March 8, 1995 is sufficient to overcome the rejection of claims 1-3, 10-12, 15, 18, 46, and 47 based upon the disclosure of Zhou et al. 1991.

12. The prior rejection of claims 1-3, 10, 11, 46, and 47 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Zhou et al. (J. Gen. Virology 71: 2185-2190, 1990) is withdrawn in view of applicants' declaration.

The declaration by Dr. Jenson under 37 C.F.R. § 1.132 filed March 8, 1995 is sufficient to overcome the rejection of claims 1-3, 10-12, 15, 18, 46, and 47 based upon the disclosure of Zhou et al. 1990.

13. The prior rejection of claims 1-3, 12, 19, 46, and 47 under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Lin et al. (Virology 187(2): 612-619, April 1992) is withdrawn in view of applicants' amendment and declaration.

The declaration by C. Richard Schlegel and A. Bennett Jensen dated June 28, 1995 under 37 C.F.R. § 1.131 is sufficient to overcome the prior art rejection over the teachings of Lin et al.

14. The prior rejection of claims 13, 14, 16, 17, 19-26 under 35 U.S.C. § 103 as being unpatentable over Zhou et al. (J. Virology 185: 251-257 1991) as applied to claims 1-3, 10-12, 15, 18, 46, and 47 above, and further in view of Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270) is withdrawn in view of applicants' declaration.

The declaration by Dr. Jenson under 37 C.F.R. § 1.132 filed March 8, 1995 is sufficient to overcome the rejection of claims 13, 14, 16, 17, 19-26 based upon the disclosure of Zhou et al. 1991 and further in view of Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270).

15. The prior rejection of claim 12-26 under 35 U.S.C. § 103 as being unpatentable over Zhou et al. (J. Gen. Virology 71: 2185-2190, 1990) as applied to claims 1-3, 10, 11, 46, and 47 above, and further in view of Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270) is withdrawn in view of applicants' declaration.

The declaration Dr. Jenson under 37 C.F.R. § 1.132 filed March 8, 1995 is sufficient to overcome the rejection of claims 12-26 based upon the disclosure of Zhou et al. 1990 and further in view of Danos et al., Schwarz et al., Cole et al.(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270).

16. The prior rejection of claims 1-3, 10-26, 46, 47, 50-58 are rejected under 35 U.S.C. § 103 as being unpatentable over Lin et al. (Virology 187(2): 612-619, April 1992) and further in view of Danos et al., Schwarz et al., Cole et al. (1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270) is withdrawn in view of applicants' amendment and declaration.

The declaration by C. Richard Schlegel and A. Bennet Jensen dated June 28, 1995 under 37 C.F.R. § 1.131 is sufficient to overcome the prior art rejection over the reference by Lin et al. and further in view of Danos et al., Schwarz et al., Cole et al.

(1986), Seedorf et al., Baker et al., Cole et al. (1987) and Danos et al. (US Patent No. 4,551,270).

NEW GROUNDS OF REJECTION

17. Claim 20-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 and dependent claims thereof are rejected for lack of antecedent basis for the term animal.

18. Claims 1-3, 10-12, and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by, or, in the alternative, under 35 U.S.C. § 103 as obvious over Browne et al. (Journal of General Virology 69(6)1263-1273).

Claims 1-3, 10-12, and 15 are rejected under 35 U.S.C. § 102(e) as being anticipated by, or, in the alternative, under 35 U.S.C. § 103 as obvious over Minson (US Patent No. 5,045,447).

Browne et al. disclose the L1 open reading frame of human papillomavirus type 16 (HPV-16) has been expressed under vaccinia virus (see abstract). Minson disclose the L1 open reading frame of human papillomavirus type 16 (HPV-16) has been expressed under vaccinia virus (see Columns 4 and 5). Browne et al. nor Minson characterize the recombinantly L1 protein as having the same properties as the claimed L1 protein (i.e. reproducing the antigenicity and conformation of the L1 on the native virus). Nevertheless, it is reasonable to conclude the protein as set forth by Browne et al. or Minson inherently has the same properties, or in the alternative similar properties as the claimed protein since both the claimed protein and protein set forth by Browne et al. or Minson are a human papillomavirus L1 protein produced recombinantly.

Neither Browne et al. nor Minson teach of the recombinant L1 produced by the same expression system (i.e. baculovirus) as claimed. However, while the proteins of the reference was not obtained from the same expression system, they nevertheless appear to be the same or an obvious or analogous variant of the proteins broadly and non-specifically claimed by applicants because they appear to possess the same or similar functional characteristics, i.e. a human papillomavirus L1 protein produced recombinantly. The source of a particular protein does not impart novelty or unobviousness to a particular protein when said protein is taught by the prior art. Since the Patent Office does not have the facilities for examining and comparing applicants' proteins with the proteins of the prior art reference, the burden is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed proteins and the proteins of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Although the references appears to disclose the same protein claimed by applicants, the references do not disclose the proteins **produced** by the claimed process. However, the production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular **process** used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, 620, 43 U.S.P.Q. 400,

402 (C.C.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (C.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979).

Browne et al. nor Minson characterize the L1 as being useful as a vaccine. However, it is the Examiner position the claim directed to a vaccine comprising the L1 is anticipated, or rendered obvious over the L1 as set forth by Browne et al. or Minson since the intended use of the claimed compositon does not carry any patentable weight.

19. Claims 13, 14, 16-26, 46, 47, and 50-58 are rejected under 35 U.S.C. § 103 as being unpatentable over Browne et al. as applied to claims 1-3, 10-12, and 15 above, and further in view of Danos et al. (US Patent No. 4,551,270).

Browne et al. teachings are set forth above. Browne et al. does not teach of a method of protecting a human against a papillomavirus infection using the L1.

Danos et al. (US Patent No. 4,551,270) teach sequences containing the L1 region are capable of producing antibodies which are able to neutralize HPV (see Columns 3 and 7). Danos et al. teach the vaccine can be administered orally or parenterally.

It would have been obvious to one of ordinary skill in the art to use the L1 as set forth by Browne et al. as a method of protecting a human against a papillomavirus infection since Danos et al. teach sequences containing the L1 region are useful as a vaccine (see Columns 3 and 7). It would have been obvious to one of ordinary skill in the art to optimize the dosage to provide the greatest protection against infection. It would have been obvious for one of ordinary skill in the art at the time of the invention to use the HPV types (i.e. HPV 18) known in the art to

protect against infection by the respective HPV since Browne et al. teaches different HPV types are associated with different clinical signs (i.e. HPV 11 and 6b are associated with benign condylomata acuminata and HPV 16, 18, and 35 are associated with invasive squamous cell carcinomas of the cervix). It would have been further obvious to one of ordinary skill in the art to include a vaccine composition which contain the L1 of several types of PV since one would have been motivated to provide protection against several types of PV described in the art.

Danos et al. (US Patent No. 4,551,270) teach (see Column 6) L1 peptides coupled to a carrier such as serum albumins preferably animal when used as a vaccine. It would have been obvious to couple L1 with serum albumins as described by Danos et al. (US Patent No. 4,551,270) such as bovine serum albumin, a serum albumin well known in the art to enhance immunogenicity of the L1.

20. Claims 1-3, 10-12, and 15 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Carter et al.

Carter et al. disclose the L1 open reading frame of human papillomavirus types 1 and 16 has been expressed in yeast (see abstract and page 515). Carter et al. does not characterize the recombinantly L1 protein as having the same properties as the claimed L1 protein (i.e. reproducing the antigenicity and conformation of the L1 on the native virus). Nevertheless, it is reasonable to conclude the protein as set forth by Carter et al. inherently has the same properties as the claimed protein since both the claimed protein and protein set forth by Carter et al. are a human papillomavirus L1 protein produced recombinantly. Furthermore, it is reasonable to conclude the protein as set forth by Carter et al. inherently, or in the alternative has the

same properties as the claimed protein (i.e. reproducing the antigenicity and conformation of the L1 on the native virus) since the L1 of HPV when expressed in yeast was identical in size the purified proteins in size and were recognized by monoclonal antibodies generated against the HPV virion (See page 520).

Carter et al. does not teach of the recombinant L1 produced by the same expression system (i.e. baculovirus) as claimed. However, while the proteins of the reference was not obtained from the same expression system, they nevertheless appear to be the same or an obvious or analogous variant of the proteins broadly and non-specifically claimed by applicants because they appear to possess the same or similar functional characteristics, i.e. a human papillomavirus L1 protein produced recombinantly. The source of a particular protein does not impart novelty or unobviousness to a particular protein when said protein is taught by the prior art. Since the Patent Office does not have the facilities for examining and comparing applicants' proteins with the proteins of the prior art reference, the burden is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed proteins and the proteins of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Although the reference appears to disclose the same protein claimed by applicants, the reference does not disclose the proteins **produced** by the claimed process. However, the production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173

USPQ 685 (CCPA 1972). Therefore, even if a particular **process** used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, 620, 43 U.S.P.Q. 400, 402 (C.C.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (C.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979).

Carter et al. does not characterize the L1 as being useful as a vaccine. However, it is the Examiner position the claim directed to a vaccine comprising the L1 is anticipated, or rendered obvious over the L1 as set forth by Carter et al. since the intended use of the claimed composition does not carry any patentable weight.

21. Claims 13, 14, 16-26, 46, 47, and 50-58 are rejected under 35 U.S.C. § 103 as being unpatentable over Carter et al. as applied to claims 1-3, 10-12, and 15 above, and further in view of Danos et al. (US Patent No. 4,551,270).

Carter et al. teachings are set forth above. Carter et al. does not teach of a method of protecting a human against a papillomavirus infection using the L1.

Danos et al. (US Patent No. 4,551,270) teach sequences containing the L1 region are capable of producing antibodies which are able to neutralize HPV (see Columns 3 and 7). Danos et al. teach the vaccine can be administered orally or parenterally.

It would have been obvious to one of ordinary skill in the art to use the L1 as set forth by Carter et al. as a method of protecting a human against a papillomavirus infection since Danos et al. teach sequences containing the L1 region are useful as a

vaccine (see Columns 3 and 7). It would have been obvious to one of ordinary skill in the art to optimize the dosage to provide the greatest protection against infection. It would have been obvious for one of ordinary skill in the art at the time of the invention to use the HPV types (i.e. HPV 18) known in the art to protect against infection by the respective HPV since Browne et al. teaches different HPV types are associated with different clinical signs (i.e. HPV 16 and 18 are associated with cancerous and precancerous lesions and HPV 6 and 11 are associated with benign condylomas). It would have been further obvious to one of ordinary skill in the art to include a vaccine composition which contain the L1 of several types of PV since one would have been motivated to provide protection against several types of PV described in the art.

Danos et al. (US Patent No. 4,551,270) teach (see Column 6) L1 peptides coupled to a carrier such as serum albumins preferably animal for use as a vaccine. It would have been obvious to couple L1 with serum albumins as described by Danos et al. (US Patent No. 4,551,270) such as bovine serum albumin, a serum albumin well known in the art to enhance immunogenicity of the L1.

22. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ghim et al. (Virology 190: 548-552 September 1992) teach (see abstract) of polyclonal and monoclonal antibodies which react specifically with conformational epitopes of the HPV-1 L1 protein. Ghim et al. teach the screening of capsid protein of PV for reactivity with conformation dependent antibodies represents a method to ensure that such proteins will be suitable for vaccine development or detection of human PV infections.

Danos et al. teach the DNA sequence encoding the L1 of HPV1a.

Schwarz et al. teach the DNA sequence encoding the L1 of HPV6b. Cole et al. (1986) teach the DNA sequence encoding the L1 of HPV33. Cole et al. (1986), Schwarz et al. further teach the strong identity (i.e. homology) of the DNA encoding the L1 of the various PV's.

Seedorf et al. teach the DNA sequence encoding the L1 of HPV16.

Baker et al. teach of the DNA sequences of the L1 of various papillomaviruses and the that DNA sequences of various papillomaviruses are available (see whole document especially page 321, Figure 17. Baker et al. teaches of using methods known in the art to determine the ORF's of particular protein including L1. Baker et al. teaches the L1 are the most highly conserved of the papillomavirus proteins (see page 379, first paragraph).

Cole et al. (1987) teaches of the DNA sequence of the L1 of HPV 18 and homology of the L1 of the various PV's.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ms. Christine Nucker, can be reached on (703)-308-4028

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-308-4227.

Anthony C. Caputa, Ph.D.
September 12, 1995

HAZEL F. SIDBERRY
PRIMARY EXAMINER
GROUP 1800